REMARKS

The undersigned wishes to thank Examiner DiBrino for granting an interview on Thursday May 24, 2006 to advance prosecution of the application.

Claims 32-42 were pending. Applicants incorporated the elements of claims 33 and 34 into claims 32 and have canceled claims 33 and 34. Applicants have canceled claim 36 without prejudice to applicant's right to pursue the canceled subject matter in a continuation application. Claims 43-46 have been added. These new claims are presented in order to more precisely define the subject matter claimed. These new claims are supported throughout the instant specification, including the original claims. In particular, support for claim 43 may be found on page 27, lines 10-14. Applicants request entry of this amendment such that claims 32, 35, 40, and 43-46 will be pending.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Claim rejections under 35 U.S.C. § 112, first paragraph – Written Description

The Office Action rejects claims 32-42 on grounds that they allegedly fail to comply with the written description requirement. In response, Applicants note that all the rejected claims have been either canceled or amended to obviate this ground of rejection.

The Office Action cited several aspects of the claims as failing to comply with the written description requirements. These will be addressed in order.

(1) The Office Action objected to the term "human." In response, applicants note that the pending claims do not recite the term "human". Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(2) The Office Action object to the recitation of "...said polypeptide consists of **an** amino acid sequence selected from..." in claim 35 on the grounds that *an* amino acid sequence would include a fragment of the sequence. In response, applicants have amended claim 35 to recite "...said polypeptide consists of **the** amino acid sequence set forth in..." to clarify the claimed subject matter. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(3) The Office Action states that the specification does not disclose which HLA-DR alleles were known at the application was filed, and merely references genetic databases. In response, applicants have amended the claims to recite specific alleles of HLA-DR. Claim 32 recites DRB1*0402, as disclosed on page 36, lines 19-21 of the originally-filed specification. Claims 44-46 recite DRB1*1501, which is disclosed on page 40, lines 3-5 of the originally-filed specification. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(4) The Office Action states that the specification fails to disclose any working examples of administration of any polypeptide to an individual *in vivo* to tolerize against an autoantigen, or to achieve a therapeutic endpoint. The Office Action cited several references in support of the assertion including Rammensee et al., Reche et al., O'Sullivan, Tisch and McDewitt, and Schwarts and Kipnis. In response, Applicants note that the claims, as amended, do not recite that the compositions are for tolerizing a human or for reaching a therapeutic endpoint. Rather, the pending claims recite a composition comprising (i) a pharmaceutically acceptable carrier, and (ii) an isolated polypeptide. In view of the amendment to the claims, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(5) The Office Action asserts that although the specification teaches the five binding pockets necessary to bind an MHC class II molecule, it does not teach the residues necessary to bind a TCR to allow tolerizing against an autoantigen of PV or MS. In response, Applicants note that the claims have been amended. The amended claims do not recite that the polypeptide must bind the TCR and thereby tolerize against an autoantigen of PV or MS. Rather, the pending claims recite a composition comprising (i) a pharmaceutically acceptable carrier, and (ii) an isolated polypeptide. In view of the amendment to the claims, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim rejections under 35 U.S.C. § 112, first paragraph – Enablement

The Office Action rejects claims 32-42 as allegedly failing to comply the enablement requirement. In particular, it alleges that the specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims.

In response, Applicants note that all the rejected claims have been either canceled or amended. Claim 36 reciting a method of tolerizing has been canceled. The remaining claims no longer make reference to a "human polypeptide," to a "pharmaceutical preparation," to an "amount...effective for tolerizing an individual to an autoantigen," or to a polypeptide that "activates autoreactive T cells from a subject having said autoimmune disease."

MPEP 2164.01 states that "when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." The claims, as amended, are directed to compositions that are not limited by a recited use. Instead of reciting a method of tolerizing, the claims recite " a composition comprising (i) a pharmaceutically acceptable carrier, and (ii) an isolated polypeptide consisting of an amino acid sequence...". Therefore, the enablement requirement is satisfied by disclosure of at least one use that would reasonably correlate with the entire scope of the claims.

The specification discloses several enabling uses for the compositions. Page 29, 3rd paragraph, describes the use of the peptides of the invention for *in vitro* assays that aid in the diagnosis and classification of pemphigus vulgaris and multiple sclerosis. Peptides which do not react with all T-cell clones from all PV patients, for example, allows an immunological classification of patients into groups according to their reactivity to the peptides. Such classification assays are common in the art (See, for example, Lin MS, *et al.* Development and characterization of desmoglein-3 specific T cells from patients with pemphigus vulgaris. *J Clin Invest. 1997 Jan 1*;99(1):31-40. **Exhibit A**). The *in vitro* assays in this paragraph of the specification extend to the use of the peptides to test the susceptibility or predisposition of a subject to an autoantigenic response. Such applications may envision *in vitro* screening of T cells from a subject against a claimed battery of peptides provided by the invention, where the more peptides the T cells react to, the greater the likelihood that the subject is predisposed to an autoantigenic response.

Moreover, page 10, lines 2-10 teach that known contact residues from a disease antigen can be incorporated into a peptide of the invention to generate peptides that induce an immune response. Similarly, the bridging paragraph between pages 33-34 recites that when the TCR-

contacting residues of a pathogen are known, they can be incorporated into the peptides of the invention to generate a vaccine.

Based on the claim amendments and the comments above, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Double Patenting Rejection

The Office Action states that Claims 32-35, 36, 41 and 42 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over Claims 3 and 4 of U.S. Pat. No. 5,874,531. Applicants note that, pursuant to 37 C.F.R. § 1.130(b), a terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome the double patenting rejection. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter.

Claim rejections under 35 U.S.C. §103

The Office Action rejects Claim 32 and 38 under 35 U.S.C. § 103(a) as being allegedly obvious over Ohashi *et al.* (*Dev. Neuroscience* **17(3)**: 189, 1995) in view of De Bruijin et al (Eur. J. Immunol).

The Office Action rejects Claim 32 and 38 under 35 U.S.C. § 103(a) as being allegedly obvious over Ohashi-Kondo in view of De Bruijin et al (Eur. J. Immunol).

The Office Action rejects Claim 32 and 38 under 35 U.S.C. § 103(a) as being allegedly obvious over Ohashi *et al.* (*J. Neuroimmunology* **54(1-2)**: 186) in view of De Bruijin et al (Eur. J. Immunol).

In response, Applicants note that claim 38 has been canceled, rendering its rejection moot. Claim 32 has been amended, in part, to recite the element previously recited in 34, *i.e.* to recite the sequence motif comprising PV motif #1 (SEQ ID NO: 21). Since claim 34 was deemed to be nonobvious over the three sets of references, incorporation of its elements into claim 32 renders claim 32 nonobvious over the references.

New claims 44-46 recite the sequence motif as being MS Motifs 1, 2, or 3 respectively. These motifs were previously listed in claim 39, now canceled. The Office Action deemed claim 39 to be nonobvious. Incorporation of the features of claim 39 into claims 44, 46 and 48 also renders these claims nonobvious.

In light of the claims amendments and the comments above, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7289.

Applicant believes no fee is due with this response in addition to those listed in the accompanying fee transmittal document. However, if an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. HUIP-P02-001, from which the undersigned is authorized to draw.

Dated: June 6, 2006

Respectfully submitted,

By _____

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